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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/007,621	12/03/2001	Susan H. Hardin	00007/02UTL	9970
23873	7590	01/17/2006	EXAMINER	
ROBERT W STROZIER, P.L.L.C			RILEY, JEZIA	
PO BOX 429			ART UNIT	
BELLAIRE, TX 77402-0429			PAPER NUMBER	

1637

DATE MAILED: 01/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/007,621	<b>Applicant(s)</b> HARDIN ET AL.	
	<b>Examiner</b> Jezia Riley	<b>Art Unit</b> 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 14 November 2005.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-10, 12-31 and 35-47 is/are pending in the application.
- 4a) Of the above claim(s) 1-6, 9, 14, 16-20, 30 and 41 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 7, 8, 10, 12, 13, 15, 21-29, 31, 35-40 and 42-47 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) 1-10, 12-31, 35-47 are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Response to Remarks***

1. Applicants' arguments, filed on 11/14/05, have been approved and entered. They have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either newly applied or reiterated. They constitute the complete set presently being applied to the instant application.

### ***Claim Rejections - 35 USC § 102/103***

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

### ***Claim Rejections - 35 USC § 103***

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 7, 8, 10, 12-13, 15, 21-29, 31, 35-40, 42-47 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Kao et al. (6,399,335 B1).

Kao et al. provides methods and compositions for polymerizing a particular nucleotide with a polymerase. In general, the method involves (a) forming a mixture of a polymerase and a nucleoside triphosphate (NTP) comprising  $\alpha$ ,  $\beta$  and  $\gamma$  phosphates and a  $\gamma$ -phosphate phosphoester-linked functional group; and (b) incubating the mixture under conditions wherein the polymerase catalyzes cleavage of the NTP between the  $\alpha$  and  $\beta$  phosphates, liberating a pyrophosphate comprising the functional group and polymerizing the resultant nucleoside monophosphate. i.e. incorporates the nucleoside monophosphate in a nascent polynucleotide. Col. 2-4.

A variety of functional groups compatible with the polymerization reaction are provided. In one embodiment, the functional group is a detectable label and the method

further comprises the step of detecting the label, wherein a wide variety of chromogenic and luminogenic labels are provided.

In another embodiment, the functional group is a cell delivery enhancing moiety, -OR, wherein R is independently selected from: substituted or unsubstituted (C1-C18) alkyl, alkenyl, alkynyl and aryl, each inclusive of carbocyclic and heterocyclic. These substituents provide enhanced therapeutic availability through enhanced gut or blood stability, cellular and/or membrane permeability, host phosphatase stability, etc. This aspect provides a wide variety of generally membrane permeable, relatively hydrophobic R substituents.

The invention provides kits for assaying polymerase reactions in standard laboratory spectrophotometers. The kits are designed so that the researcher can replace one or more components with the sample they wish to test.

Col. 4 shows exemplary of detectable label (Table 1A (4aminophenol for example) and labeled NTP's (Table 1B). see also col. 7-12 . Which are viewed to be inclusive of the instant claims 23-26 for example.

5. Claims 7, 8, 10-13, 15, 21-24, 27-29, 31-33,36-40, 42-44, 47 are rejected under 35 U.S.C. 102(a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Williams (WO 00/36151).

Williams et al. provide assay methods for the detection of pyrophosphate cleavage, which is advantageous in number of biological reactions. For example, in DNA polymerase reaction (pages 7-8). William et al. discloses a method comprising the

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step of adding a modified nucleotide having a  $\gamma$ -phosphate with a fluorophore moiety attached thereto (pages 4-5, 16). Said method comprising a nucleotide polymerizing agent (polymerase). Further page 19 discloses that there are many linking moieties and methodologies for attaching fluorophore to nucleotides. Figure 4 shows the preferred linkers, which is viewed to be inclusive of instant claim 24. Additionally page 21 shows that the linker can comprised aryl groups (line 13). Suitable fluorophore include EDANS, (page 17, last paragraph). Page 7 shows that suitable NTPs include ATP. Williams et al. provides kits and integrated for practicing the assays (page 5). The polymerase is a DNA polymerase such as DNA polymerase I, II, or III, for example (page 8).

6. Response to Applicant's Arguments:

Applicant argues that the references do not teach fidelity incorporation. Additionally Applicant states that "the discovery allows simple modified nucleotides to be used in sequencing reactions to decrease the number of incorrect reading and mismatched and thereby reducing error rates and increasing sequencing read confidences". This is not convincing because even though the references do not mention such term they are directed to the addition of modified nucleotide comprising molecular tag to a nucleotide polymerization medium. It is obvious and inherent that one of ordinary skill will use modified nucleotide to increase or decrease incorporation of nucleotide in a polymerase reaction in order to study the effectiveness of polymerization agent and therefore improving such reaction.

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As it is pointed in *In re Fitzgerald* (205 USPQ), page 594, 2nd col., 1st full paragraph, supports the shifting of the burden of proof to the applicant that the instantly claimed invention is novel and unobvious over the prior art. Since both the prior arts and the instant application prepare and use composition which appeared to be identical, the prior arts therefore suggest that the composition therein disclosed are effective in assay for determining incorporation fidelity using modified nucleotides, suggesting the instant application under 35 U.S.C. § 103(a).

7. **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire **THREE MONTHS** from the date of this action. In the event a first response is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than **SIX MONTHS** from the date of this final action.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jezia Riley whose telephone number is 571-272-0786. The examiner can normally be reached on 9:30AM - 5:00PM.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Wednesday, January 11, 2006

  
JEZIA RILEY  
PRIMARY EXAMINER